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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/948,149	10/09/1997	BRIAN M. FENDLY	11669.266USU2	6683

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EXAMINER	
SWARTZ, RODNEY P	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
04/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/948,149	FENDLY ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36,39,43 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-36,39,43 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 January 2008 has been entered.

Claims 28-31, 37, 38, 40, 42, 44, 45, 49, 50, 52-57, 59, 61, and 62 have been canceled. Claims 32, 33, 34, 35, 36, 39, 43, and 51 have been amended.

2. Claims 32-36, 39, 43, and 51 are pending and under consideration.

Rejections Moot/Withdrawn

3. The rejection of claims 28-31, 37, 38, 40, 56, and 57 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) is moot in light of the cancelation of the claims.

4. The rejection of claims 28-31, 37, 38, and 40 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) is moot in light of the cancelation of the claims.

5. The rejection of claims 42, 44, 45, 49, 50, 52-55, 59, 61, and 62 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) in view of Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) and Fendly et al (*Cancer Research*, 50:1550-1558, 1990), and further in view of Deshane et al (*J. Invest. Med.*, 43(Suppl. 2):328A, 1995), and Senter et al (U.S. Pat. No. 4,975,278) is moot in light of the cancelation of the claims.

6. The rejection of claims 42, 44, 45, 59, 61, and 62 under 35 U.S.C. 112, second paragraph, as being indefinite is moot in light of the cancelation of the claims.

7. The rejection of claim 43 under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in light of the claim amendments.

Rejections Maintained

8. The rejection of claims 32-36, 39, 43, and 51 under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990), Deshane et al (*J. Invest. Med.*, 43(Suppl. 2):328A, 1995), and further in view of Senter et al (U.S. Pat. No. 4,975,278) is maintained.

Applicants argue that although Shepard et al and Lewis et al disclose multiple anti-ErbB2 antibodies, neither reference discloses use of the recited first and second antibodies in a combination treatment. The other references do not remedy the deficiencies of Shepard et al and/or Lewis et al.

The examiner has considered applicants' arguments, but does not find them persuasive. The instant specification, page 13, lines 3-13 teaches the "7C2/7F3 epitope on ErbB2 (i.e. any one or more of residues in the region from about residue 22 to about residue 53 of ErbB2 (SEQ ID NO:2))" and the "4D5 epitope of ErbB2 (i.e., any one or more residues in the region from about residue 529, e.g. about residue 561 to about residue 625, inclusive (SEQ ID NO:4)). Thus, the two antibodies fit the requirements of the claims in question.

Shepard et al teach the monoclonal anti-HER2 antibody (4D5) which: a) inhibits the growth of SKBR3 breast tumor cells in cell culture by 66% (Abstract; Table II); b) enhances the sensitivity of SKBR3 cells to cisplatin (Figure 5); and c) enhances the sensitivity of SKBR3 cells

to TNFt~ (Figure 4). Shepard et al also teach monoclonal anti-HER2 antibodies 7C2 and 7F3 which bind to Domain 1 of ErbB2 (Figure 2; page 119, section Derivation of muMab 41)5) and which inhibit SKBR3 proliferation by 21% and 38% respectively (Table II).

Lewis et al also teach the monoclonal anti-HER2 monoclonal antibodies 4D5, 7C2, and 7F3, which inhibit human tumor cells (Table 2) and mediate antibody-dependent cellular cytotoxicity (Figure 4).

Fendly et al teach the production and characterization of the monoclonal anti-HER2 antibodies utilized by Shepard et al and Lewis et al (Abstract; page 1550-1552, section Materials and Methods).

Deshane et al teach that intracellular antibody knockout of the ErbB2 oncoprotein achieves targeted eradication of tumor targets by induction of apoptosis.

Senter et al teach a method for delivery of cytotoxic drugs to tumor cells by using a tumor specific antibody/enzyme conjugate that binds to the tumor cells, and upon additional administration of a prodrug, the enzyme converts the prodrug to an active cytoxic drug (Abstract; Figure 1; column 4, line 5 to column 5, line 4).

Thus, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to use the monoclonal anti-HER2 monoclonal antibodies, such as 4D5, 7C2, and 7F3, as taught by Shepard et al, Lewis et al, and Fendly et al to induce cell death in cells overexpressing ErbB2 receptor by a variety of methods and in a variety of sequential administrations to induce cell growth inhibition/death. Likewise, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to enhance the efficacy of the monoclonal antibodies by using the reagents and techniques taught by Senter et

al, or by using in concert with the monoclonal antibody treatment, radiation treatments as widely used in the treatment of tumors.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Wednesday from 9:00 AM to 7:30 PM EST. Thursday is the examiner's work at home day.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Shannon Foley, can be reached on (571)272-0898.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rodney P. Swartz, Ph.D./

Primary Examiner, Art Unit 1645

April 14, 2008